

Figure 1

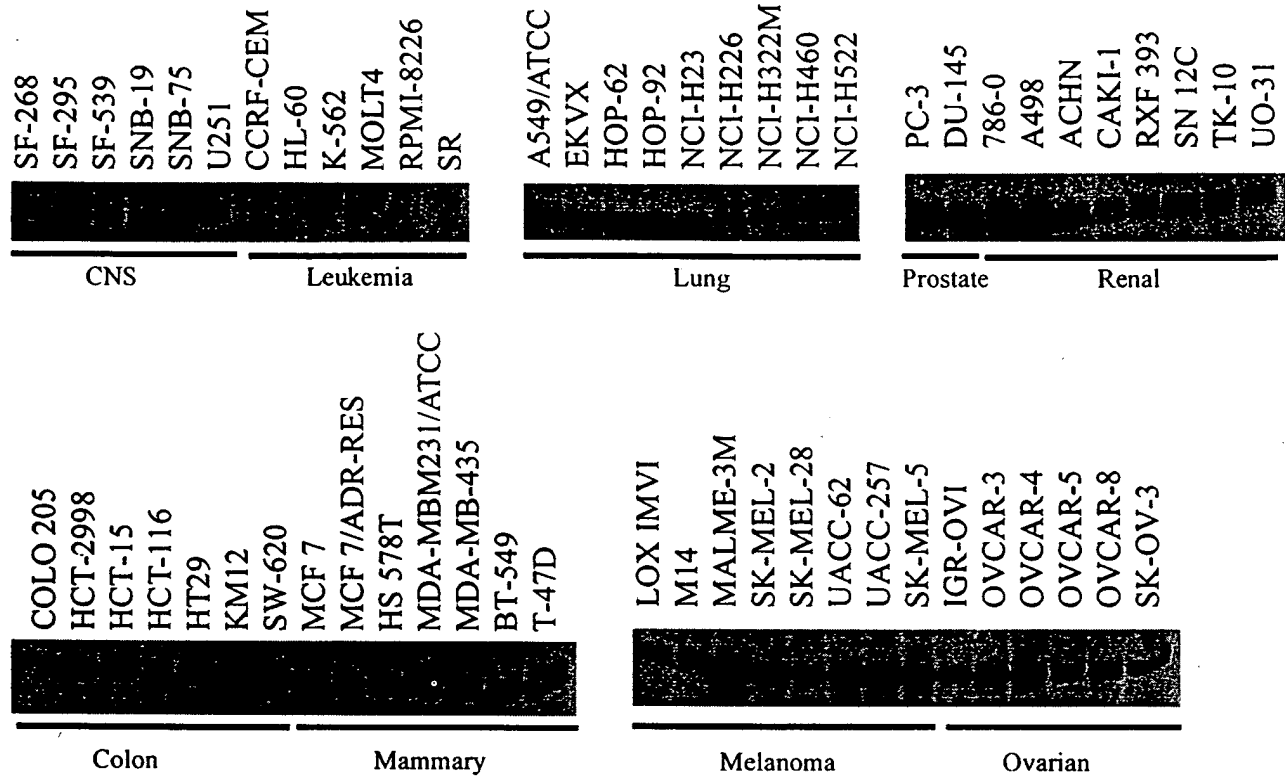


Figure 2

BEST AVAILABLE COPY

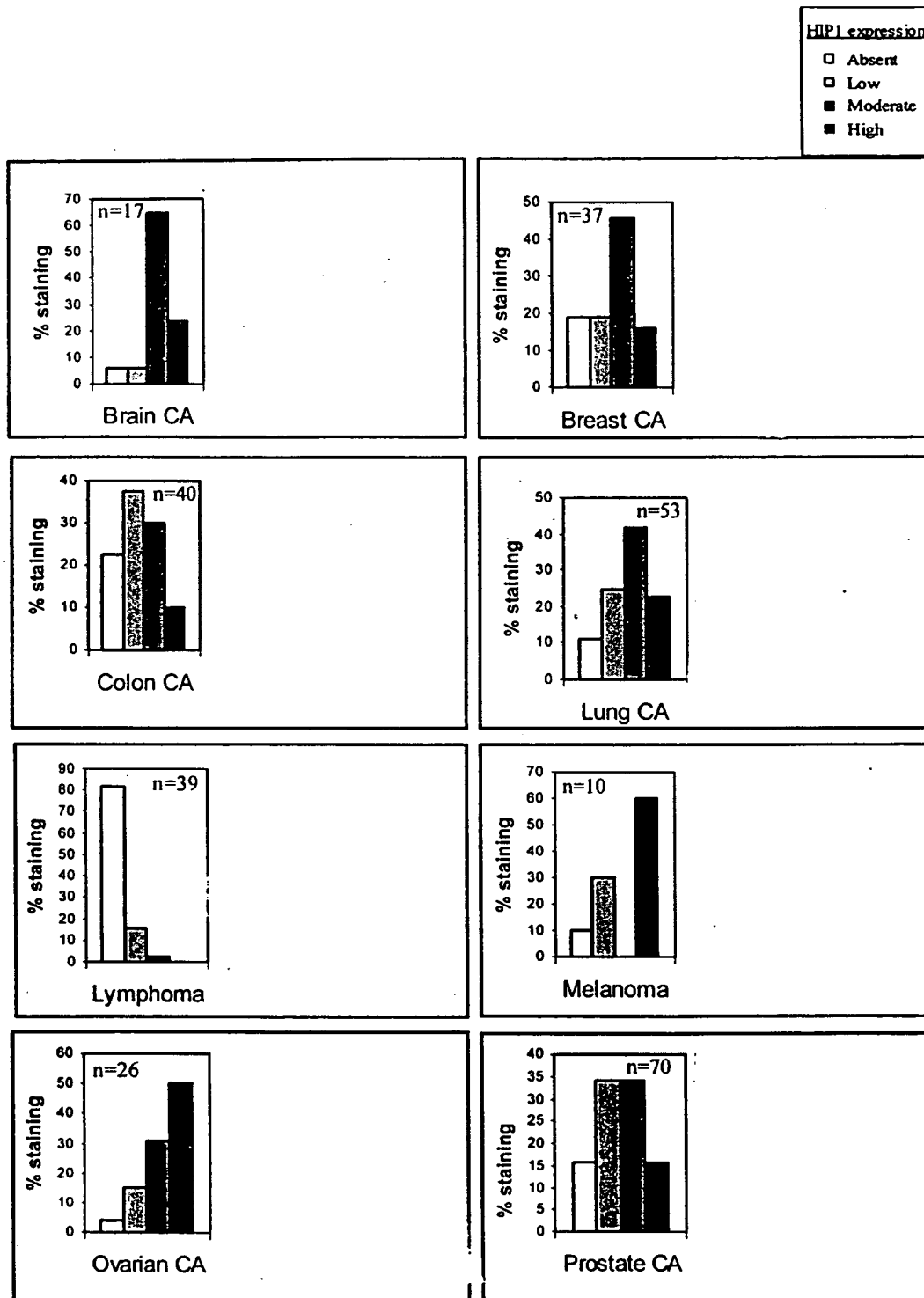
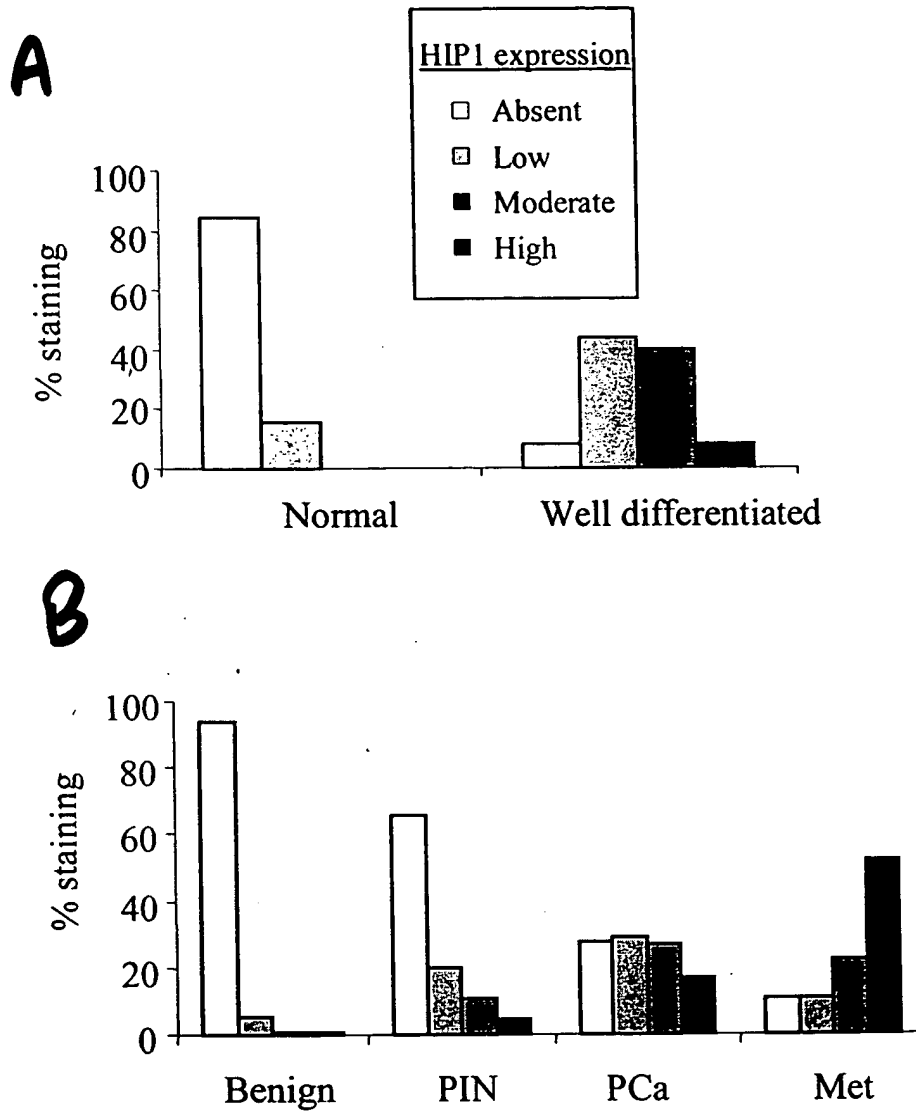


Figure 3



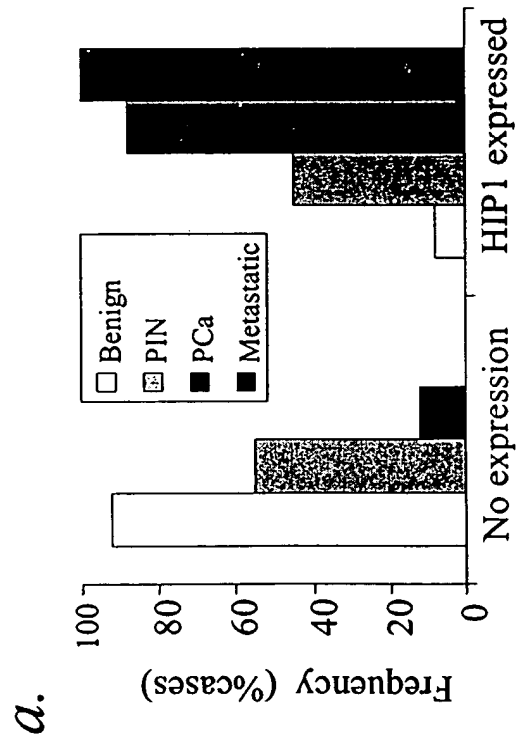
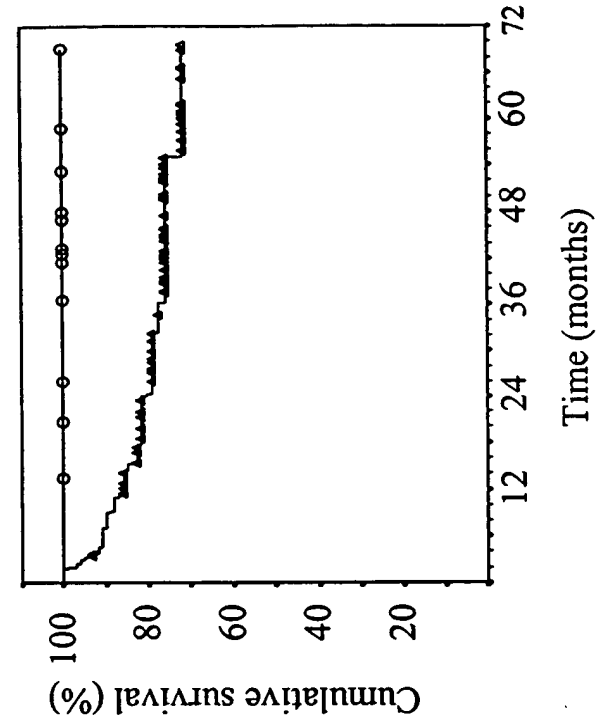


Figure 4

Figure 5

		HIP1 xpression				Total
		Absent	Low	Moderate	High	
ID #	21	6				6
	22		2			2
	23	1	1	1		3
	25	1	3			4
	26		2	1		3
	31			3	1	4
	32		1	2	1	4
	33				2	2
	38	1		1	4	6
	43		2	2	1	5
	44	2	2			4
	45		2			2
	53		1	2	1	4
	56			2		2
	58			3	1	4
	62	1		1	2	4
	63			5	1	6
	65	1	1	1	2	5
	66	1	1	1		3
	67	2	1		1	4
	70	2	1	2		5
	73		1	6		7
	75	2				2
	76	1	3	1		5
	77	3	1			4
	78	1	2			3
	82	1	2			3
	83	1	1	1	3	6
	84	2	1	1	2	6
	85	1	3	1		5
	89	1	1	3	1	6
	91			4		4
	92	1	1	1		3
	93		1	2	2	5
	96	2	1	1	2	6
	97	1	2	1		4
	99			2	2	4
	101		2	4		6
	102	4			1	5
	103		4			4
	105		2	1		3
	106	1	1		1	3
	108		1	2	3	6
	109		1	5		6
	110	3				3
	111	4	1			5
	113	2		2		4
	114	2				2
	115				2	2
	117			2		2

		HIP1 expression				Total
		Absent	Low	Moderate	High	
ID #	118		1	3		4
	119		2	3	2	7
	123	3	3	1		7
	125	4	2			6
	127	3	1			4
	128			1	3	4
	129	3	1			4
	131	1	1			2
	132			3	1	4
	141			2	2	4
	142	2	3			5
	144	1	3	2	1	7
	145	2				2
	153		1	1		2
	154	2				2
	155				4	4
	159	4	2			6
	161	2				2
	162	1	1	1		3
	164			1	3	4
	165		4	2		6
	169		2			2
	170	3	2	1		6
	171			2		2
	172	2				2
	173	3		1		4
	175	3				3
	177	4	2			6
	178	2	1			3
	179	3	1			4
	180	1			3	4
	181	4				4
	182	2				2
	183		2			2
	186		4			4
	194	4	1			5
	194	2	1			3
	195	1	5	1		7
	199		1	1	1	3
	204		3	1		4
	205			2	2	4
	206		6			6
	207		4			4
	208			3	1	4
	209			2	3	5
	212	1	4	1	3	9
	213	2	3	2		7
	214		1	1	3	5
	217		1	2	3	6
	218	1	6			7

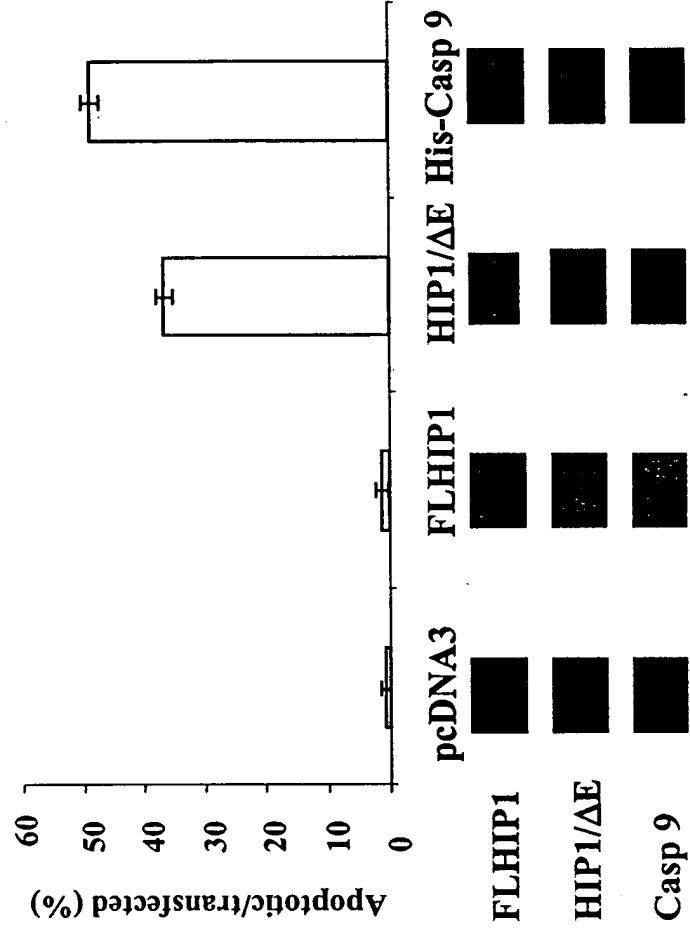
		HIP1 expression				Total
		Absent	Low	Moderate	High	
ID #	220		1		5	6
	225		1	3		4
	228			3		3
	229	1		2	1	4
	230	2				2
	231			2	1	3
	234			2		2
	235		3	1		4
	236	2	3			5
	237	4	1			5
	238	2				2
	239		3	2		5
	241	2	1	1		4
	248			2		2
TOTAL		128	136	123	76	463

Figure 6

**A**



**B**



**Figure 7**  
**Full length HIP1 (SEQ ID NO:1)**

ccaagcttgggtacccccggggcagccgagggccctgactcggtcctcgggcgacatggatcggatggc  
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acgaggtcggagaaagtgcgtgaacaacttttcccaggttaacagtgagatgtttgactacctggagtgt  
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## Figure 8

### Full length HIP1 (SEQ ID NO:2)

MDRMASMKQVPNPLPKVLSRRGVGAGLEAAERESFERTQTVSINKAINTQEVAVKEKHARTCILGTHHEK  
GAQTFWSVNNRLPLSSNAVLCWKFCVFKLLRDGHPNVLKDSLRYRNELSDMSRMWGYLSEGYGQLCSIY  
LKLLRTKMEYHTKNPRFPGNLQMSDRQLDEAGESDVNNFSQLTVEMFDYLECELNLFQTVFNSLDMSRSVS  
VTAAGQCRLAPLIQVILDCSHLYDYTVKLLFKLHSCLPADTLQGHRDRFMEQFTKLKDLFYRSSNLQYFKR  
LIQIPQLPENPPNFLRASALSEHISPVVVIAPAEASSPDSEPVLEKDDLMDMDASQQNLFDNKFDDIFGSSF  
SSDPFNFSQNGVKNDEKDHLIERLYREISGLKAQLENMKTESQRVVLQLKGHVSELEADLAEQQHLRQQA  
ADDCEFLRAELDELRRQREDTEKAQRSLSIEIERKAQANEQRYSKLKEYSELVQNHADLLRKNAEVTQVS  
MARQAQVDLEREKKELEDSELRISDQGQRKTQEQLVLESLKQELATSQRELQVLQGSLETSAQSEANWAA  
EFAELEKERDSLVSAGAAHREEELSALRKELQDTQLKLASTEESMCQLAKDQRKMLLVGSRKAAEQVIQDAL  
NQLEEPPLISCAGSADHLLSTVTSISSCIEQLEKSWSQYLACPEDISGLLHSITLLAHLTSDAIAHGATTC  
LRAPPEPADSLTEACKQYGRETAYLASLEEESLENADSTAMRNCLSKIKAIGEELLPRGLDIKQEELGD  
LVDKEMAATSAAIETATARIIEEMLSKSRAGDTGVKLEVNERILGCCTSLMQAIQVLIIVASKDLQREIVESG  
RGTASPKEFYAKNSRWTEGLISASKAVGWGATVMVDAADLVVQGRGKFEELMVCSEIAASTAQLVAASKV  
KADKDSPNLAQLQQASRGVNQATAGVVASTISGKSQIEETDNMDFSSMTLTQIKRQEMDSQVRVLELENEL  
QKERQKLGEELRKKHYELAGVAEGWEEGTEASPTLQEVVTEKE\*SQTNTPYVSVNPNPCYLSRVCFPSHRPN  
PWSPRGSHTTAITQCRGHA\*HFQRLPP\*RHPFCLDPWISTASYGGWLGFLVLFFFKFHSHSLSQRAHPW  
G\*VSRAPQLW\*LQRWCCPGLSVLHLRLHTDQVLAHPVHAPGSGGAAE\*QLSSKSRRRVSAFPS\*S\*IPAES  
LCPPLQGRRQKEGQEGSHSPVPVTRLKNLITCLNGAGEINNTTSLPE\*TVREWSLSSGSPPLAQRRSVGV  
IPNSFLQTSALASS\*IGRSFHLLRN\*QTRKIRCNCSSHQRTLYLVCYP\*YLLLTSLKQQQPTKRCLEQSEL  
QV\*L\*QSSSFCPATSAFKNQKKGQAGLLLTWIPKQGDHLELLGQRK\*ERTEPAAPTFFSHMPQALAALWT  
G\*GQRAHEQLARDGQPNSTFPLLDGPQHLSDLLILGKQRLPSLSIATHWW\*PSSTSEFLQGRPLEHAXEG  
P

(\* are stop sequences)

**Figure 9**  
**Delta ENTH (SEQ ID NO:3)**

gttaacagtggagatgtttgactacctggagtgtgaactcaacctcttccaaacagtattcaactccctgg  
acatgtcccgtctgtgtccgtgacggcagcagggcagtgccgcctcgccccgctgatccaggtcatcttg  
gactgcagccacctttatgactacactgtcaagcttctcttcaaactccactcctgcctcccagctgacac  
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## Figure 10

### Delta ENTH (SEQ ID NO:4)

MFDYLECELNLFQTVFNSLDMSRSVSVTAAGQCRLAPLIQVILDCSHLYDYTVKLLFKLHSCLPADTLQGH  
RDRFMEQFTKLKDLFYRSSNLQYFKRLIQIPQLPENPPNFLRASALSEHISPVVVIPAEASSPDSEPVLEK  
DDLMDMDASQQNLFDNKFDDIFGSSFSSDPFNFSQNGVNKDEKDHLIERLYREISGLKAQLENMKTESQR  
VVLQQLKGHVSELEADLAEQQHLRQQAADDCEFLRAELDELRRQREDTEKAQRSLSIEIERKAQANEQRYSKL  
KEYSELVQNHADLLRKNAEVTQVSMARQAQVDLEREKKELEDSELERISDQGQRKTQEQLEVLESLSKQEL  
ATSQRELQVLQGSLETSAQSEANWAAEFAELEKERDSLVSAAHREEELSALRKELQDTQLKLASTEESMC  
QLAKDQRKMLLVGSRKAAEQVIQDALNQLEEPPLISCAGSADHLLSTVTSISSCIEQLEKSWSQYLACPED  
ISGLLHSITLLAHLTSDAIAHGATTCLRAPPEDSLTEACKQYGRETLAYLASLEEEGSLENADSTAMRN  
CLSKIKAIGEELLPRGLDIKQEELGDLVDKEMAATSAAIETATARIIEEMLSKSRAGDTGVKLEVNERILGC  
CTSLMQAIQVLIVASKDLQREIVESGRGTASPKIFYAKNSRWTEGLISASKAVGWGATVMVDAADLVVQGR  
GKFEELMVCSEHIAASTAQLVAASKVKADKDSPNLAQLQASRGVNQATAGVVASTISGKSQIEETDNMDF  
SSMTLTQIKRQEMDSQVRVLELENELOKERQKLGE LRKKHYELAGVAEGWEEGTEASPPTLQEVVTEKE\*S  
QTNTPYVSVNPCYLSRVCFPSHRPNPWSPRGSHTTAITQCRGHA\*HFQRLPP\*RHPFCCLDPWISTASYGG  
WLGFLVLFFFFKFHSHSLSQRAHPWG\*VSRAPQLW\*LQRWCCPGLSVLHLRLHTDQVLAHPVHAPGSGGA  
AE\*QLSSKSRRRVSAFPS\*S\*IPAESLCPPLOGRRQKEGQEGSHSPVPVTRLKNLITCLNGAGEINNTTS  
LPE\*TVREWSLSSGSPPLAQRSSVGVI PNSFLQTSALASS\*IGRSFHLLRN\*QTRKIRCNC SHQGR TLYLV  
CYP\*YLLLTSLKQQPTKRCLEQSELQV\*L\*QSSSFCPATSAFKNQKKGQAGLLLTWIPKQGDHLELLGQ  
RK\*ERTEPAAPT PFSHMPQALAAALWTG\*GQRAHEQLARDGQPNSTFPLLDGPQHLSDLLILGKQRLPSLSI  
ATHWW\*PSSTSEFLQPGRPLEH

(\* are stop sequences)

h1

Figure 11

# Domain Structure of HIP1

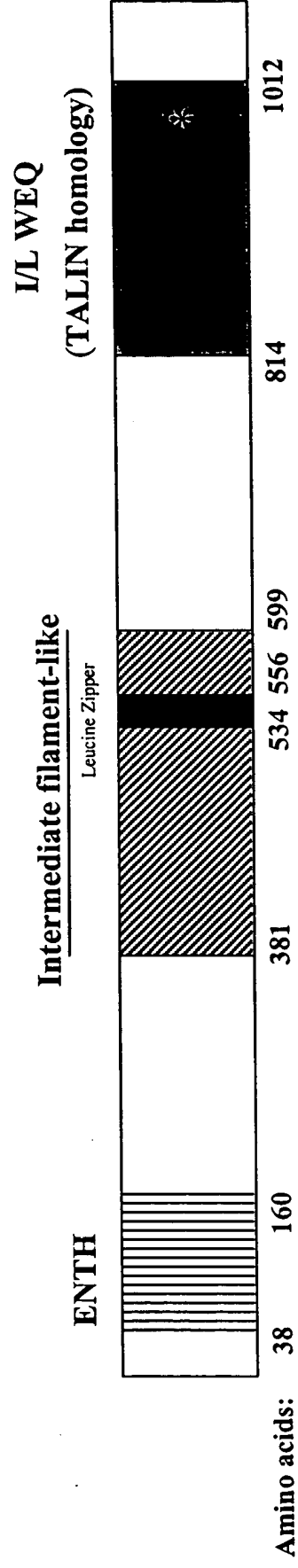
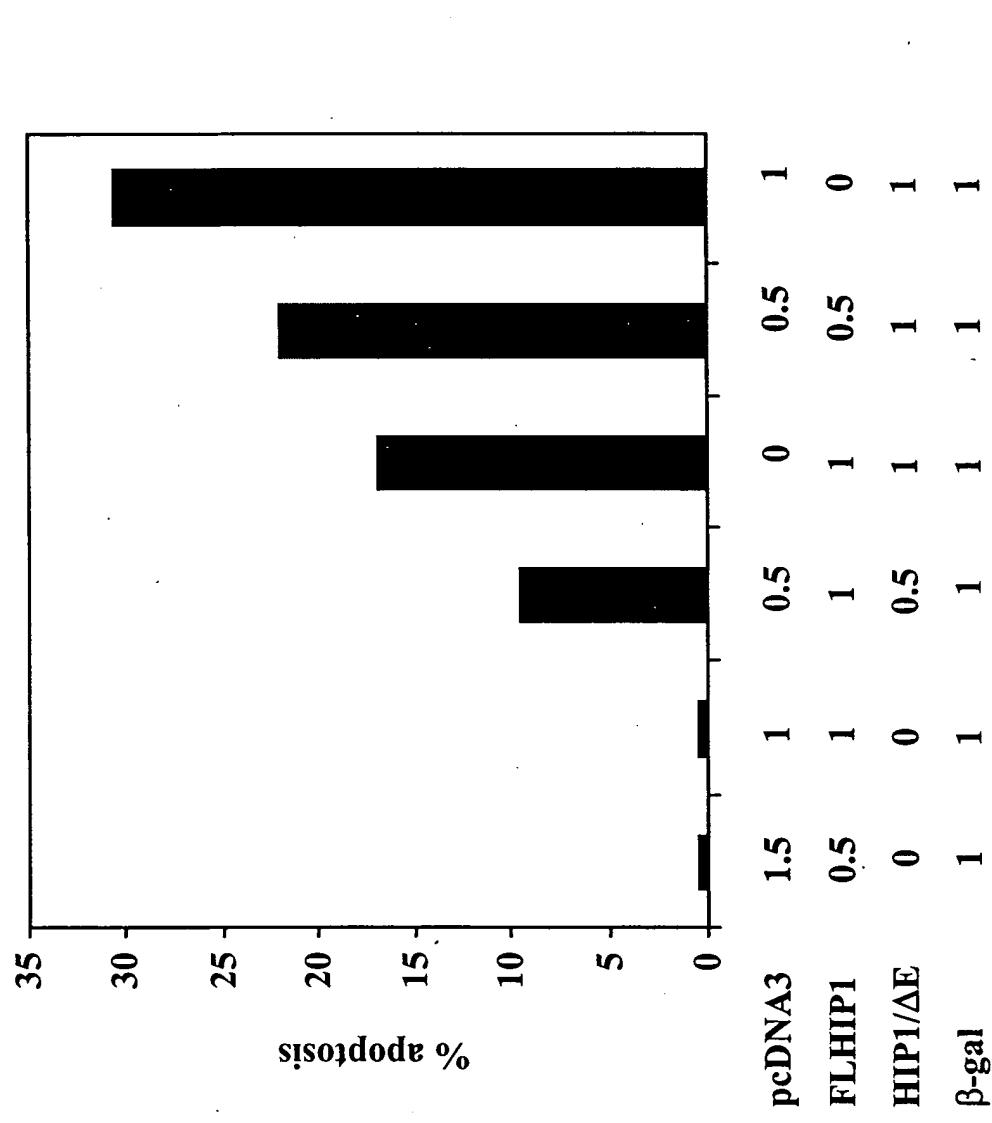


Figure 12

# Rescue of apoptosis caused by $\Delta E$ with FLHIP1



18 h post-transfection

Figure 13

# Rescue only with Akt/Dncasp9

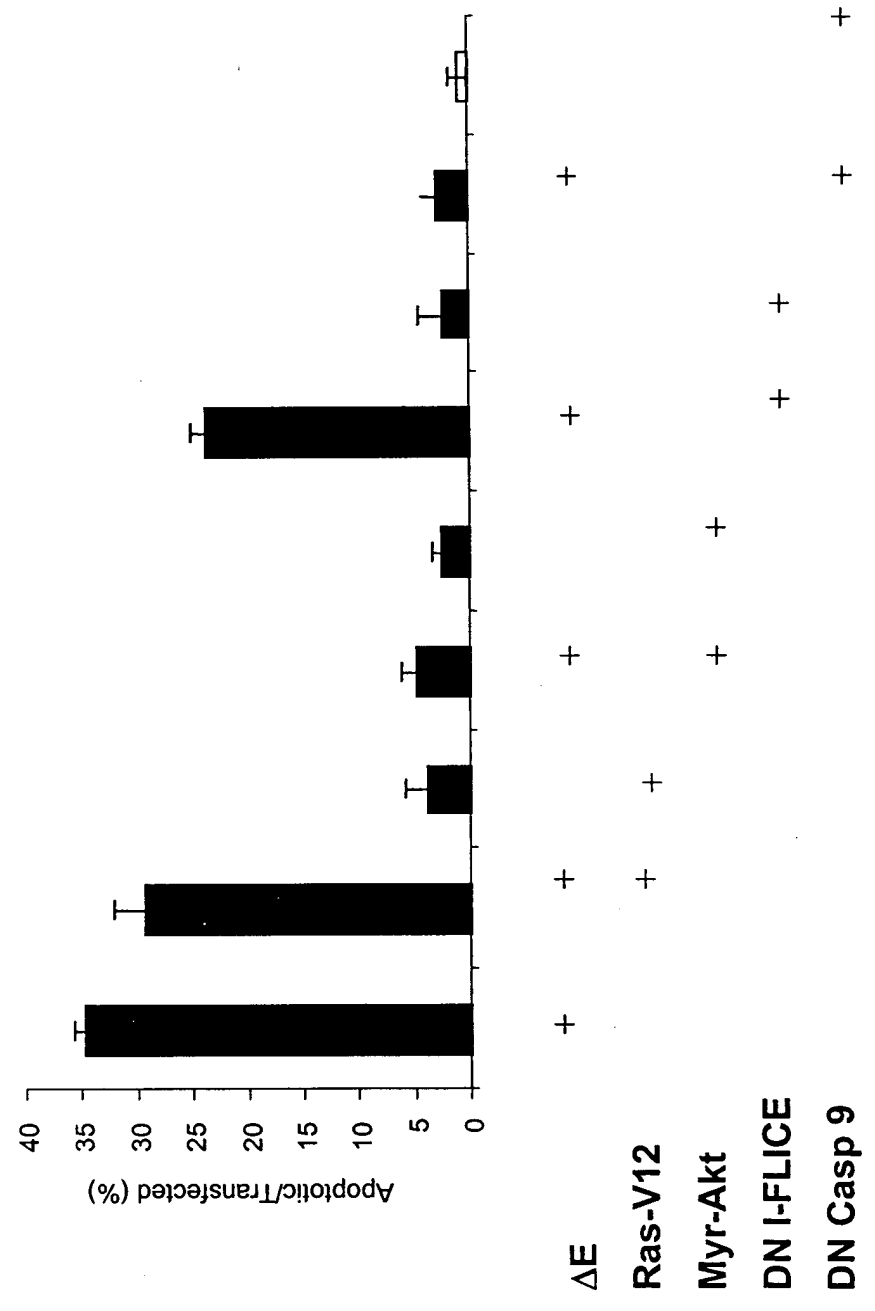
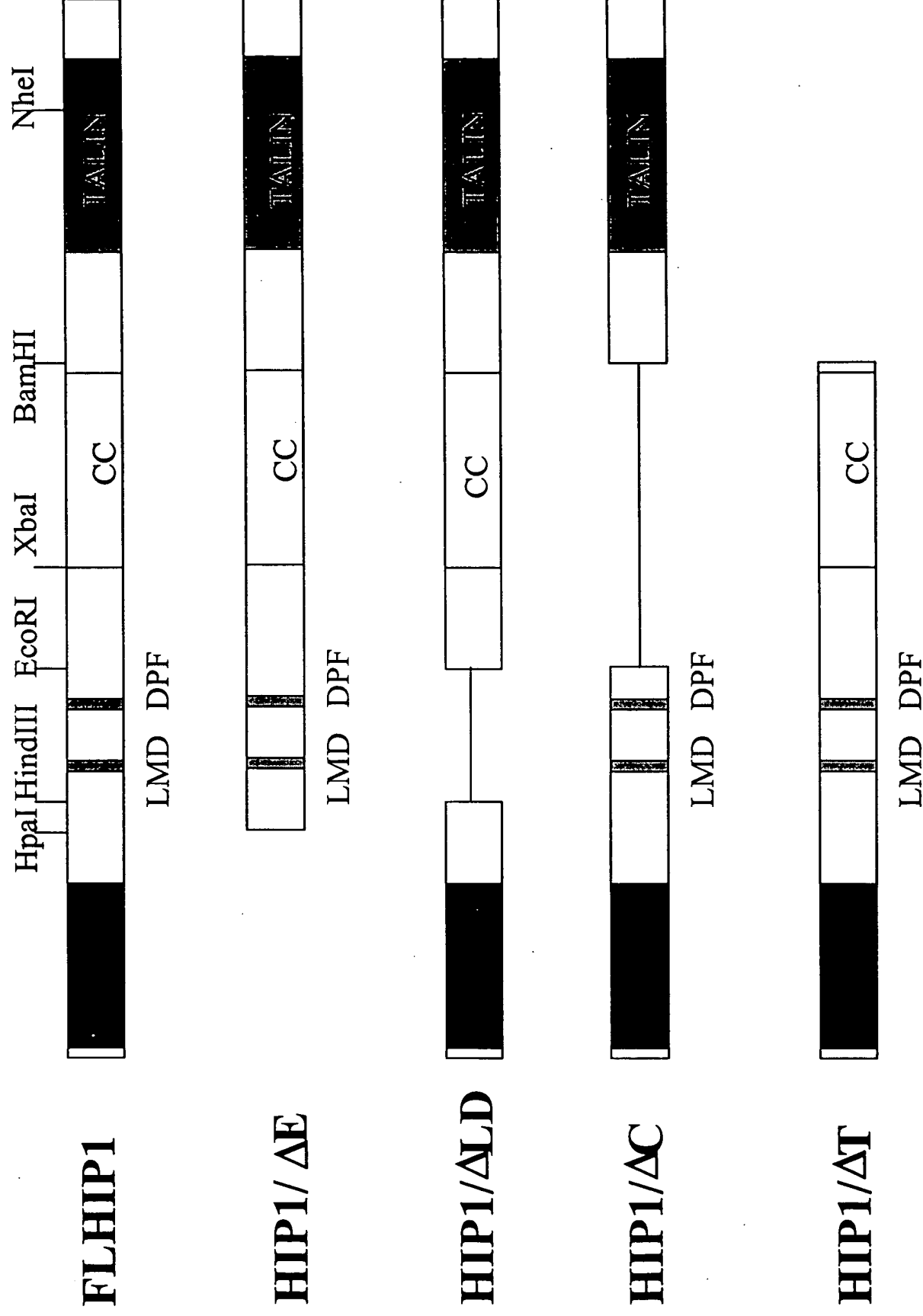


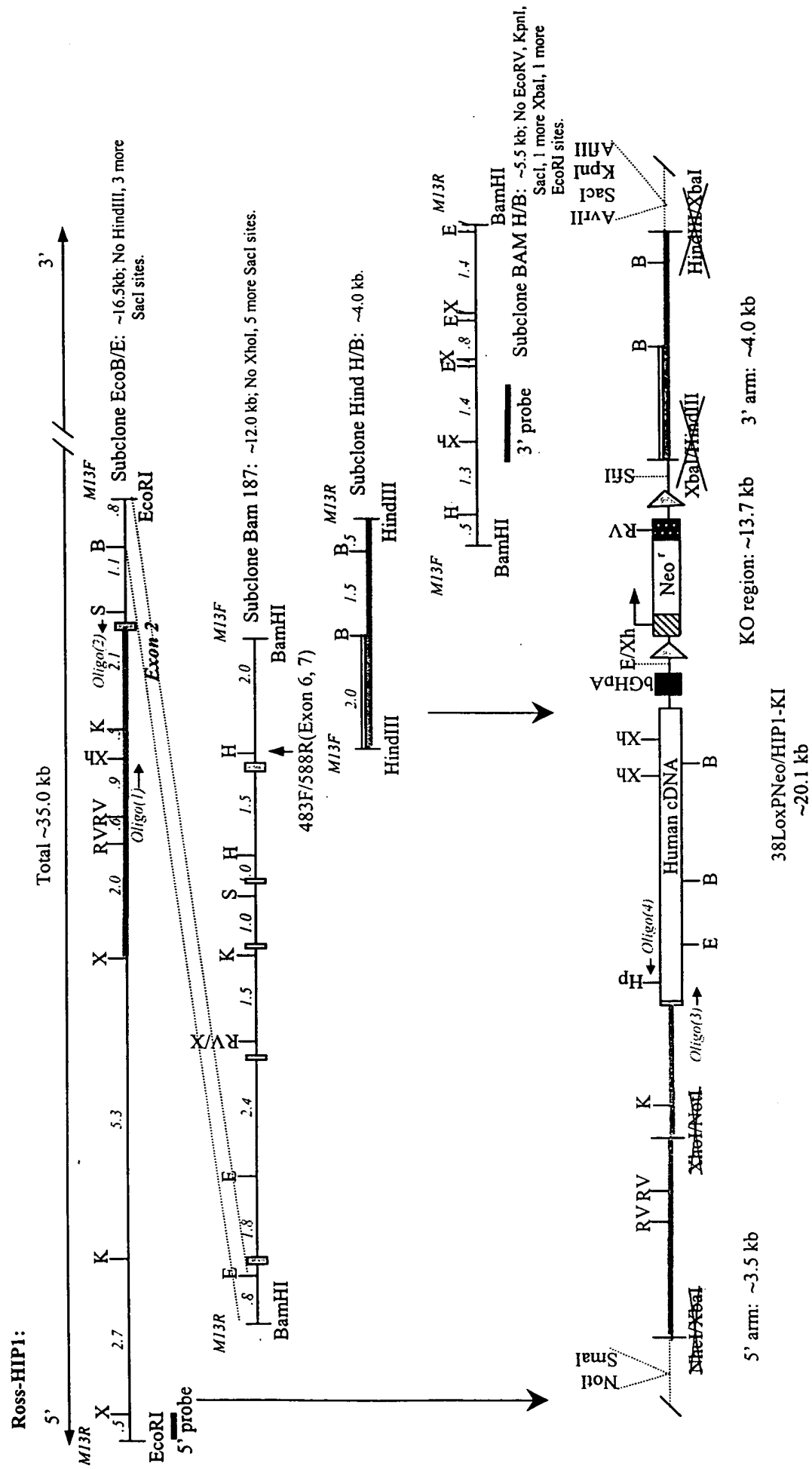


Figure 14

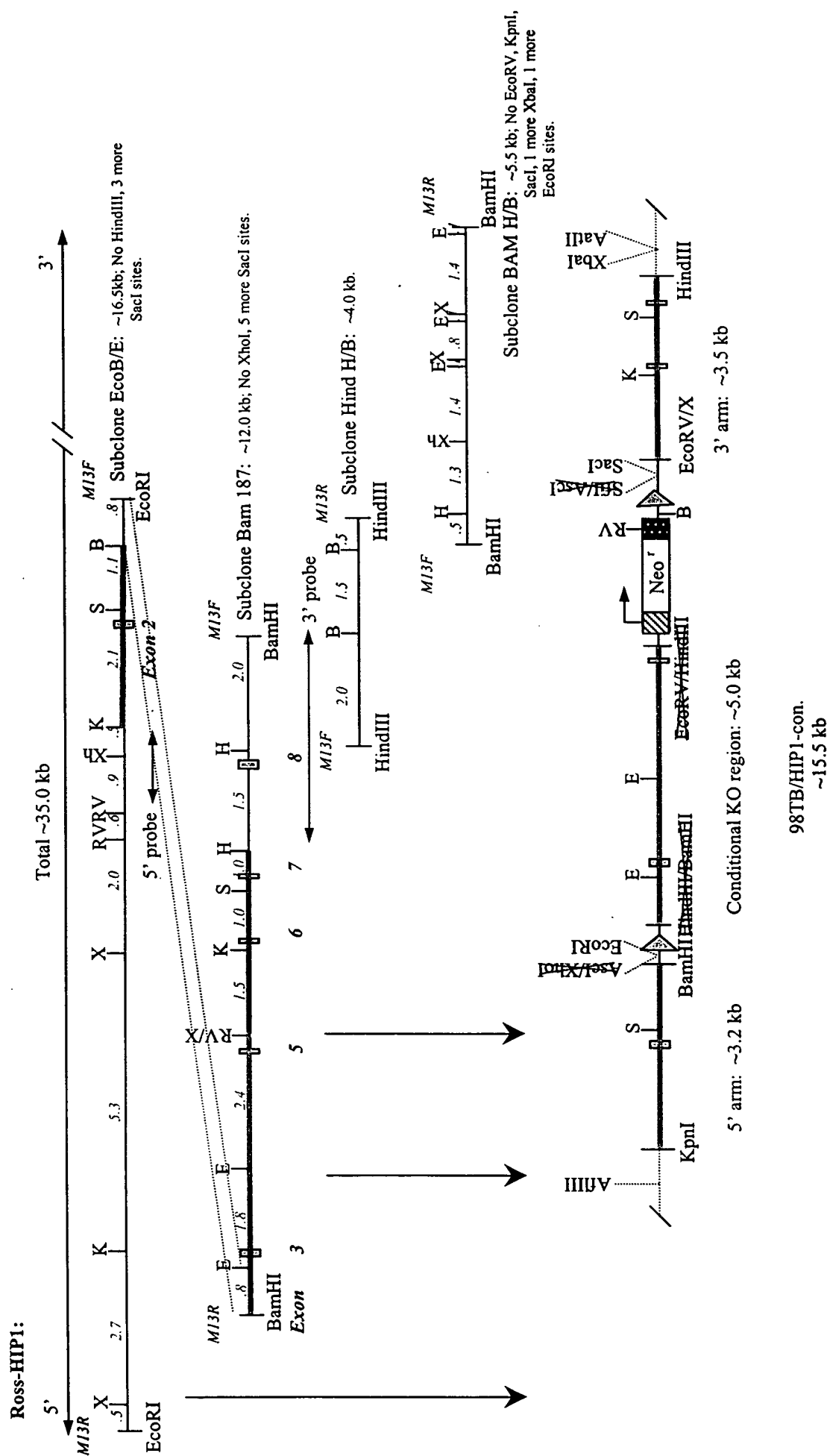


# Figure 15

## Vector Construction Strategy for HIP1/PDGFβR knock-in



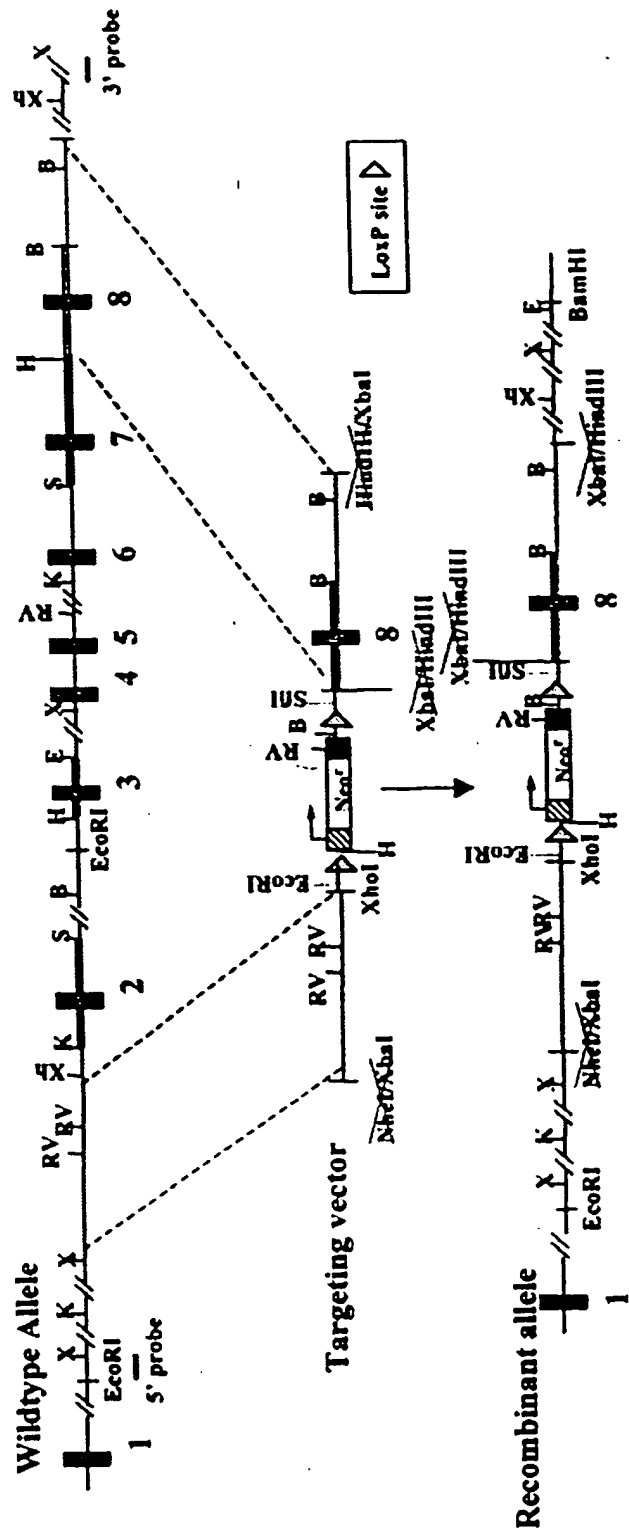
## Vector Construction Strategy for conditional HIP1 knock-out



## Figure 17

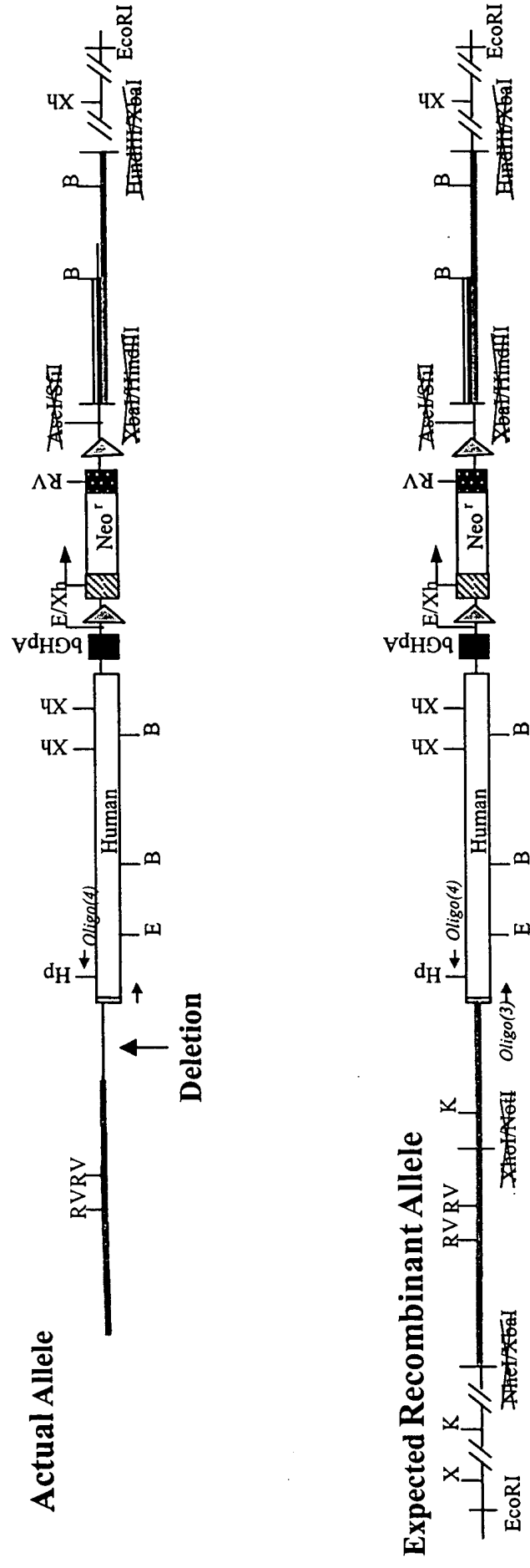
-173 GGGCCGAGCCAGCGGAGGGGCTCCTGAAGGGGCGGGGGCGGGCGGGGAAGCCGT  
-119 TCGGCGAGGGGCGGGGTCTCTGGAAGACTGGCAGAACTCACAGCCAATGGCAGGC  
-64 GGGAGCCGTCCCGTTAGCGCCGGATCCCCGCGGGTAGGGCGGGGCGGGCGGCGCC  
-10 GTGGGGATCC  
exon 1 0 CGGGGCAGCCGAGGGCCCCCTGACTCGGCTCCTCGCGGCGACATGGATCGGATGGCCA  
57 GCTCCATGAAGCAGGTGCCCAACCCACTGCCCAAGGTGCTGAGCCGGCGCGGGGTCC  
114 GCGCTGGGCTGGAGGCGGCGGAGCGCGAGAGCTTCGAGCGGAC TCAGGT.....  
.....TCAG  
exon 2 161 ACTGTCAGCATCAATAAGGCCATTAAACGCAGGAAAGTGGCTGTAAAGGAAAAACATGCC  
222 AG

Figure 18



# Figure 19

## Deletion of the HIP1/PDGFβR knock-in ES cell allele



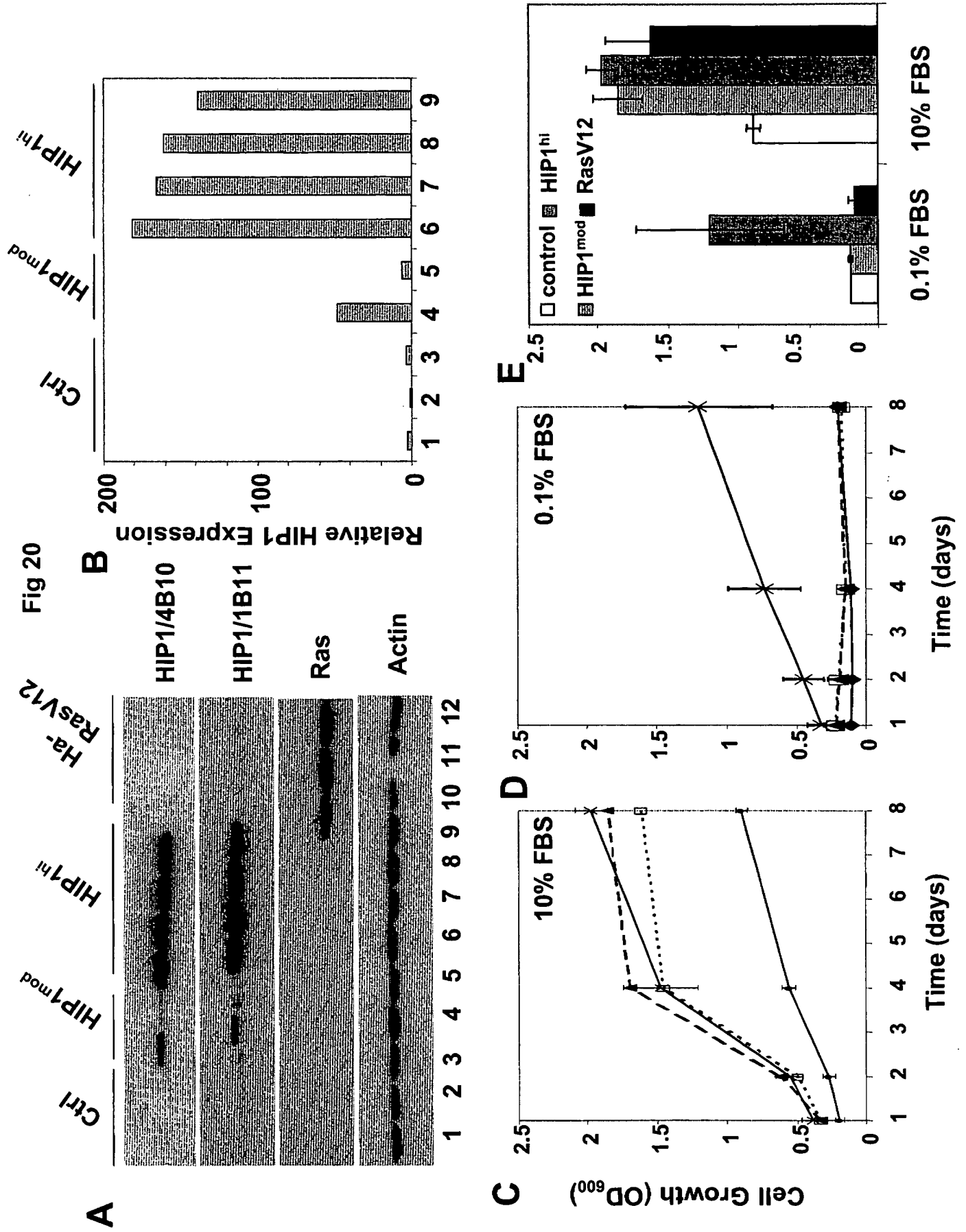


Fig 21

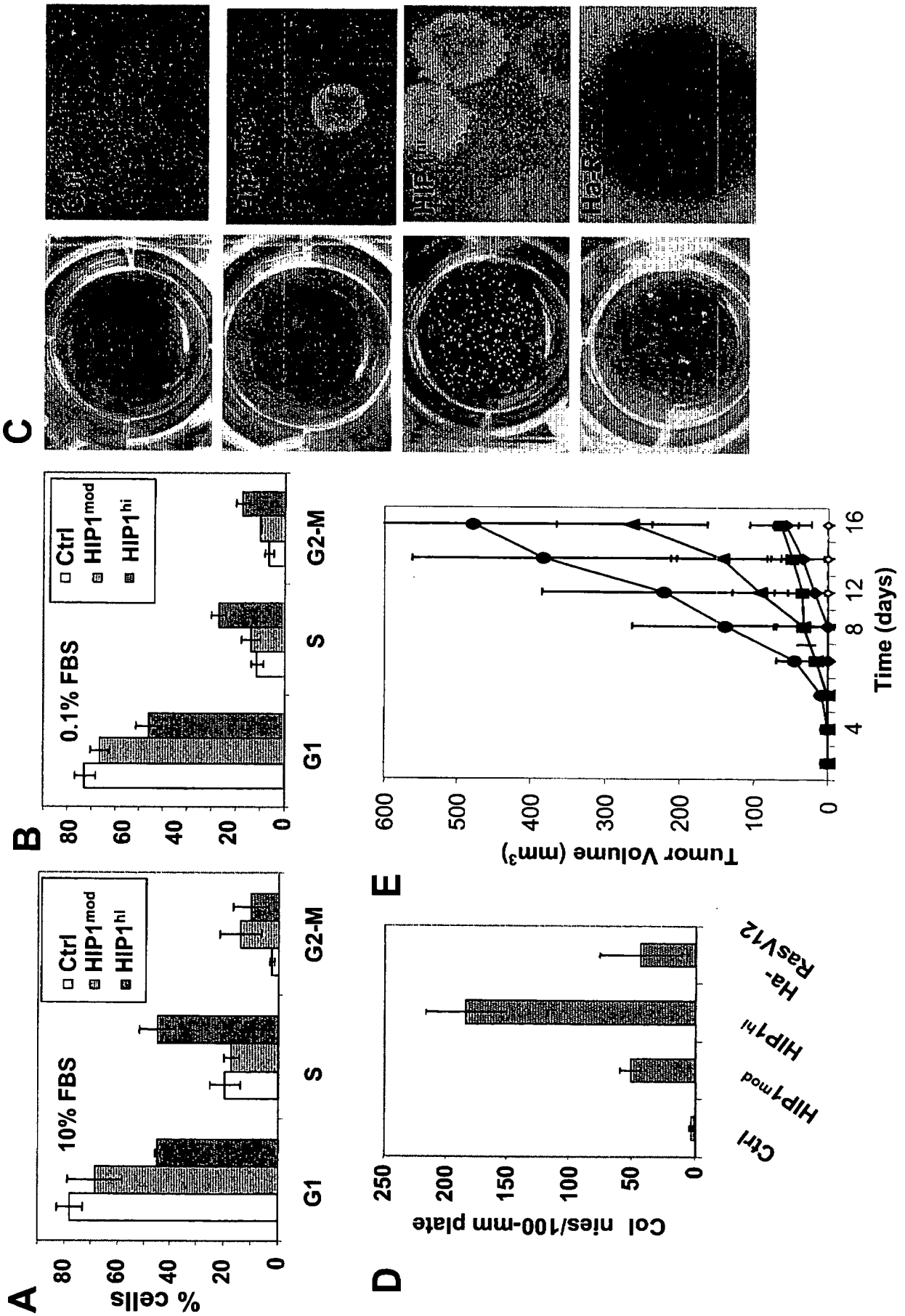




Fig 22

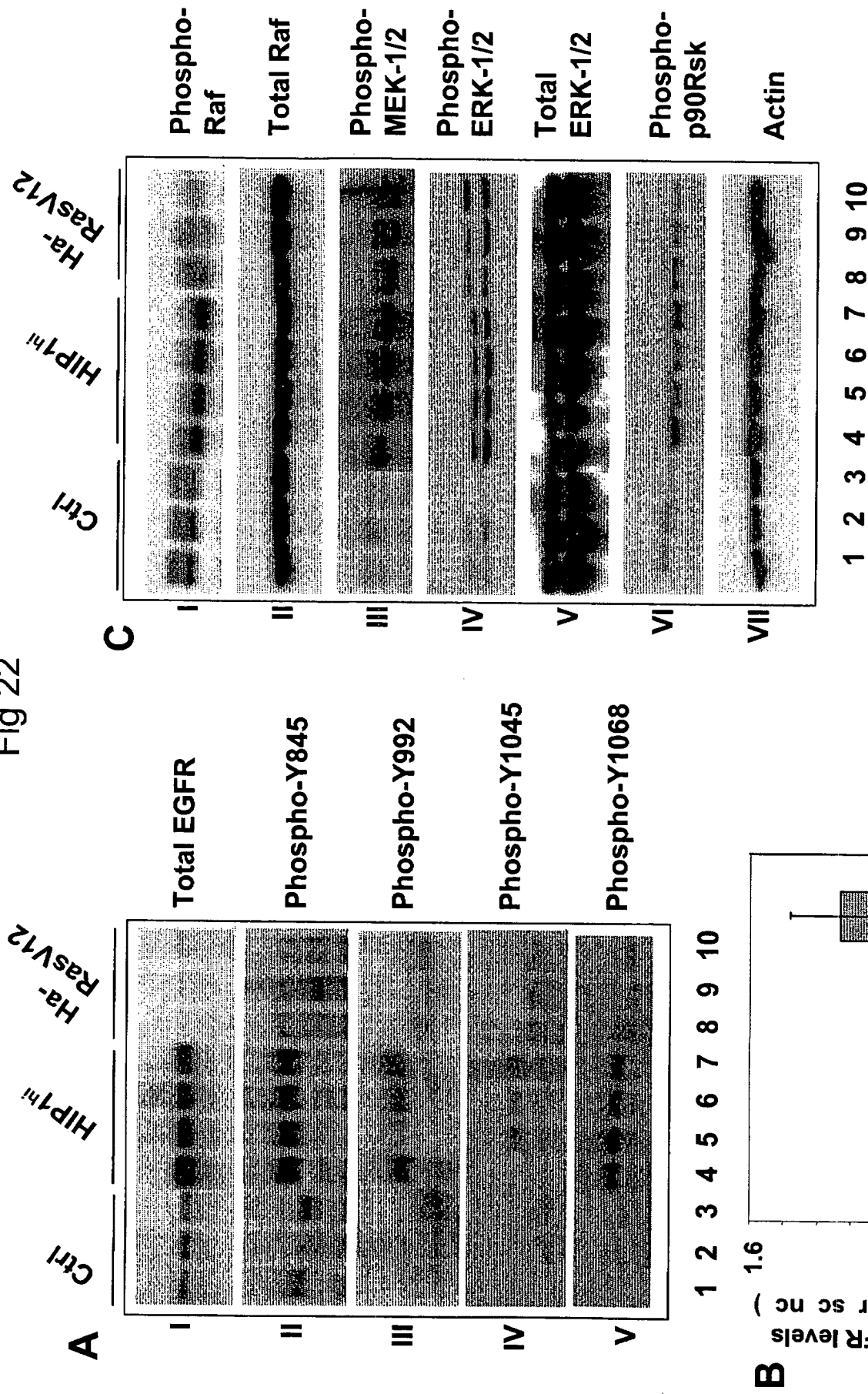


Fig 23

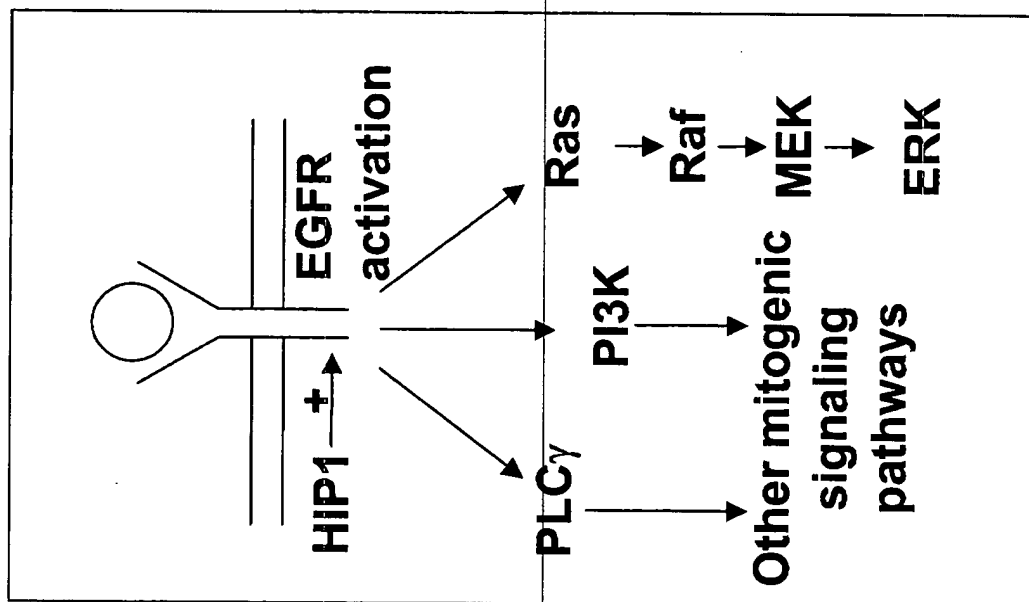


Fig 24

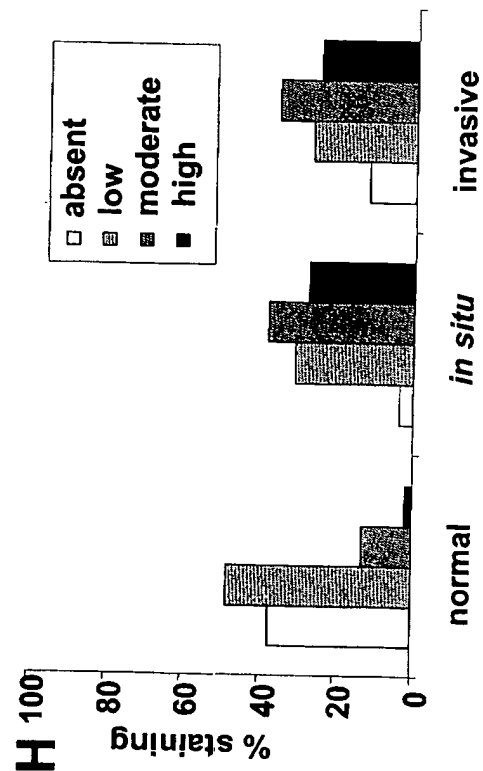
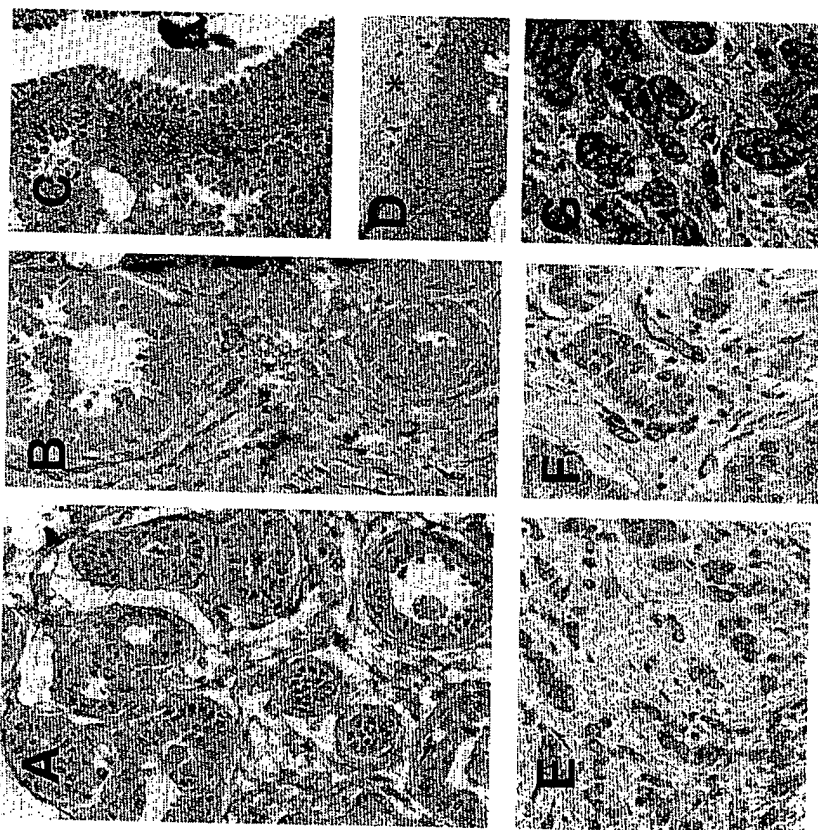
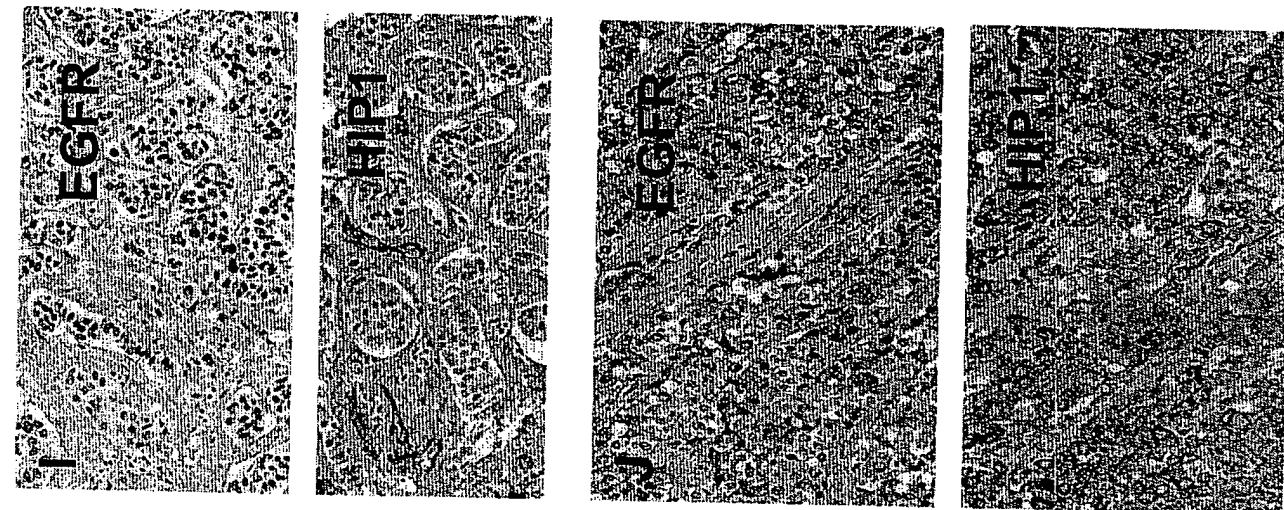
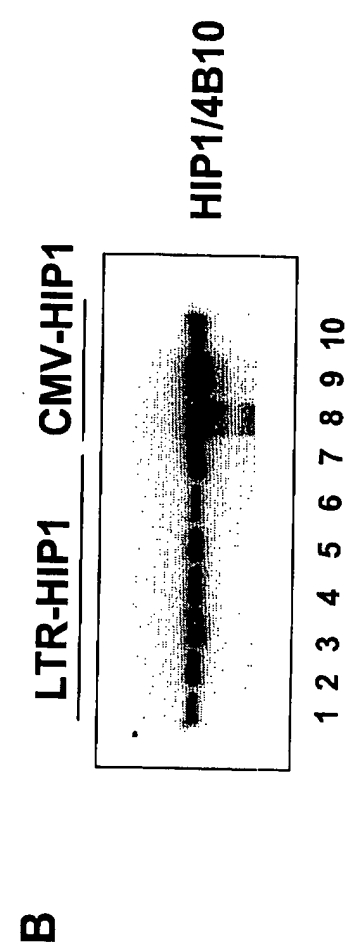
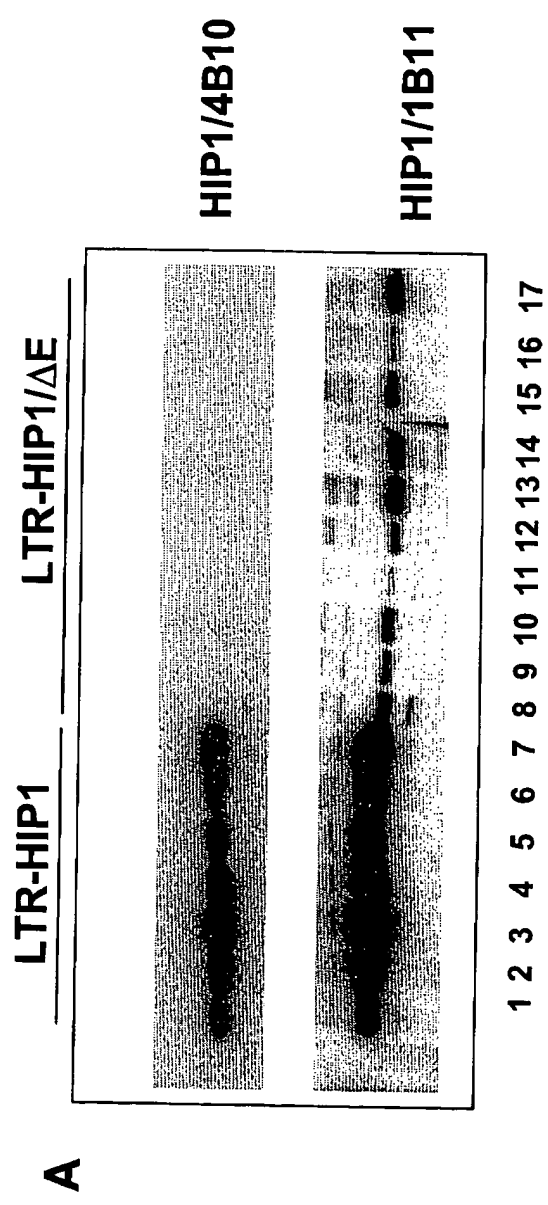


Fig 25



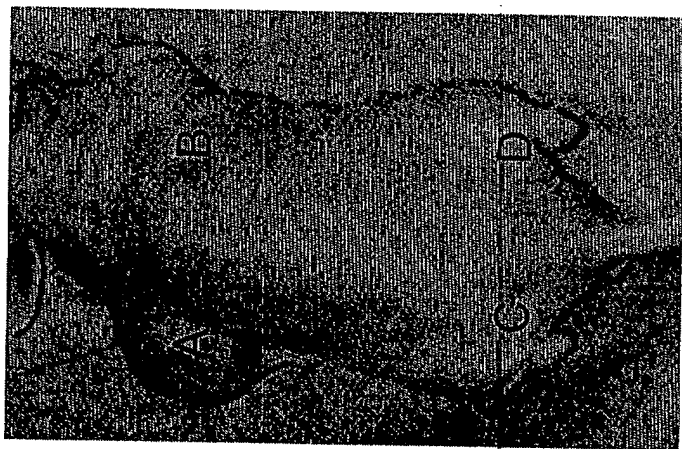
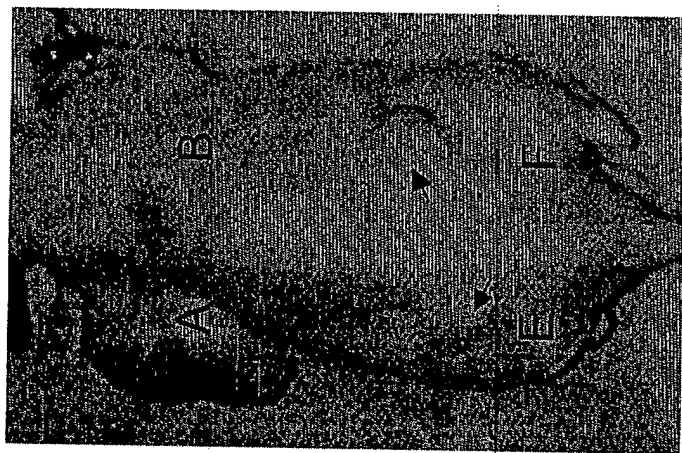
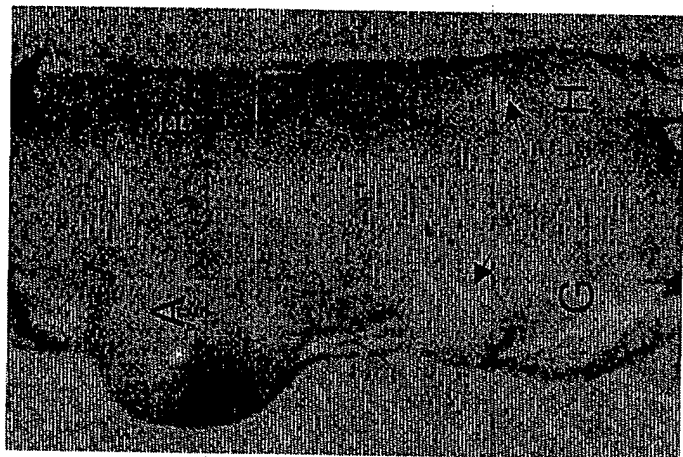
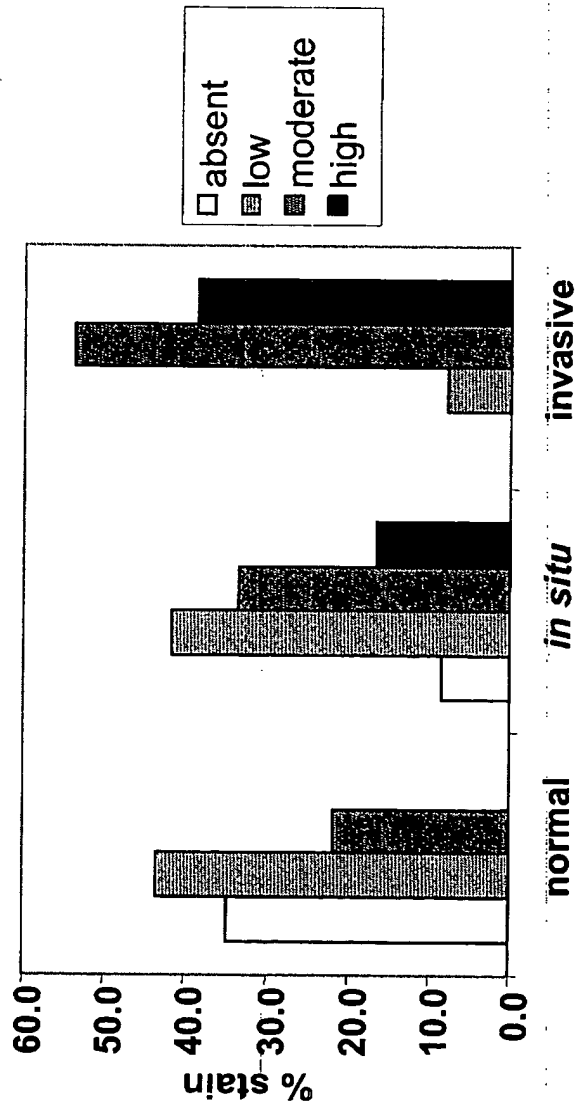


Fig 26

Fig 27

A



B

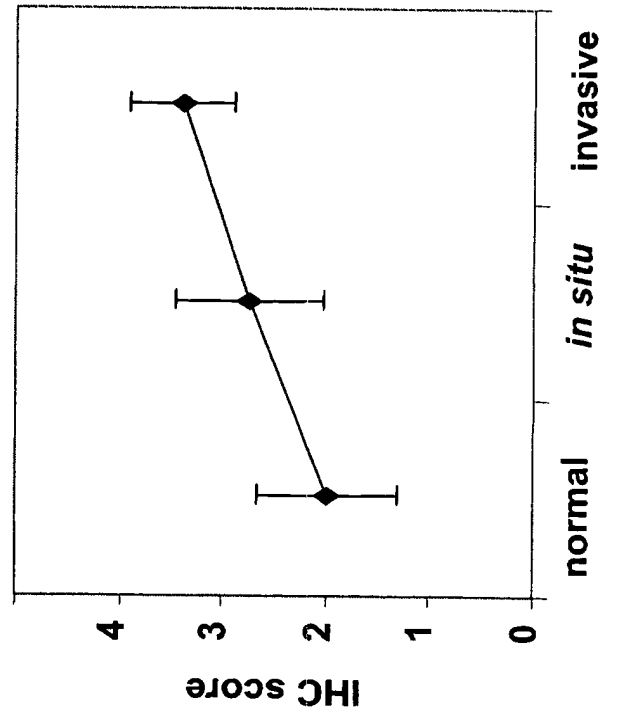


Figure 28

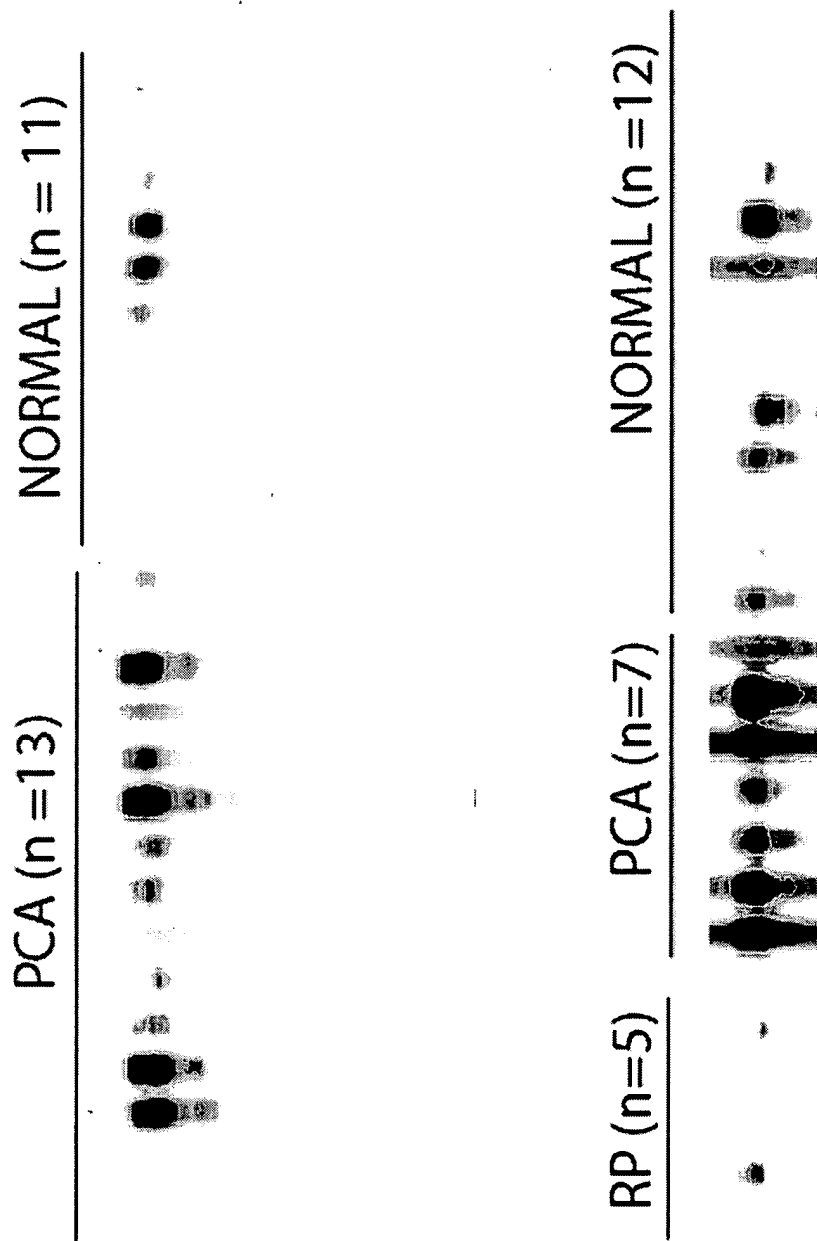


Figure 29

